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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,563	O'KEEFE ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/4/04; 11/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11 are pending and under examination.

Information Disclosure Statement

2. The Information Disclosure Statements (IDS) filed 04 June 2004 and 14 November 2005 have been considered by the Examiner. A signed copy of the IDS is included with the present Office Action.

Specification

3. The disclosure is objected to because of the following informalities:

a. The specification discloses SEQ ID NO:110 as an amino acid sequence (page 7, line 20) and as a nucleic acid sequence (page 7, line 14). Clarification is requested.

b. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. For example, at page 7, line 3 a space needs to be inserted between the terms "SEQ" and "ID". Applicant's cooperation is requested in reviewing correcting any errors of which applicant may become aware in the specification.

c. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title should be limited to "Humanized anti-CCR2 Antibodies".

Appropriate correction is required.

Claim Objections

4. Claim 1 is objected to because there is no space between the term "immunoglobulin" and the term "heavy".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a humanized immunoglobulin or antigen-binding fragment thereof having specificity for CCR2 comprising the heavy chain variable region sequence of SEQ ID NO:17 and the light chain variable region sequence of SEQ ID NO:12 or a humanized immunoglobulin having specificity for CCR2 comprising the heavy chain variable region sequence of SEQ ID NO:17 and the constant region sequence of SEQ ID NO:110 (human IgG1 constant region) and the light chain variable region sequence of SEQ ID NO:12 and the light chain constant region sequence of SEQ ID NO:112 (human Ck), does not reasonably provide enablement for a humanized immunoglobulin heavy chain or humanized immunoglobulin light chain having specificity for CCR2 that do not contain a full set of 6 CDRs, three from the variable heavy domain and three from the variable light domain or a humanized immunoglobulin or antigen-binding fragment thereof having specificity for CCR2 comprising the heavy chain

variable region sequence of SEQ ID NO:17 and the light chain variable region sequence of SEQ ID NO:12 and a portion of the human constant region of SEQ ID NO:110 as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention is drawn to engineered anti-CC-chemokine receptor 2 (CCR2) antibodies, where the relative skill of those in the art is deemed to be high.

The claims are drawn to humanized immunoglobulin heavy chains and humanized immunoglobulin light chains and fragments thereof having specificity for CCR2 and a humanized immunoglobulin or antigen-binding fragment thereof comprising the heavy and light chain variable regions (i.e., SEQ ID Nos:17 and 12, respectfully) and a portion of the human heavy chain constant region (SEQ ID NO:110). Thus, the claims are broadly drawn to humanized immunoglobulin heavy chains and humanized immunoglobulin light chains that do not contain the full set of 6 CDRs, three from the VH and three from the VL domains and do not bind antigen and humanized antibodies

comprising just any portion of the human IgG1 heavy chain constant region of SEQ ID NO:110.

The specification discloses only humanized immunoglobulins that contain both a heavy chain variable domain and a light chain variable domain and bind CCR2 (see Example 2 and Fig. 25), the same antigen as the parental immunoglobulin that contributes the CDRs (i.e., CDRs of monoclonal antibody 1D9) (see Examples 2-4). Further, the specification teaches a humanized anti-CCR2 antibody that contains the human IgG1 constant region and human kappa constant region in its native form (see Example 3). The specification does not teach or provide working examples of humanized immunoglobulins comprising just any portion of the human IgG1 constant region wherein the humanized immunoglobulins bind CCR2. Further, the specification does not teach humanized immunoglobulin heavy chains or humanized immunoglobulin light chains, which do not contain a full set of six CDRs, three from the variable heavy domain and three from the variable light domain and bind antigen, i.e., CCR2. There are no working examples of humanized immunoglobulin heavy chains or humanized immunoglobulin light chains that bind CCR2. Thus, the teachings provided in applicant's specification are limited relative to the broad scope of the subject matter embraced by the present claims.

The state of the prior art is such that it is well established in the art that the formation of an intact antigen-binding site of all antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the

contact residues for the binding of the antibody to its target epitope (Paul, Fundamental Immunology, (textbook), 1993, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions" Ids reference AMM filed 6/4/04). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites (Paul, page 293, first column, lines 3-8 and line 31 to column 2, line 9 and lines 27-30). Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA 1982 Vol. 79:1979-1983, 1982, Ids reference ANN filed 6/4/04). Rudikoff et al teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Coleman P. M. (Research in Immunology, 145:33-36, 1994) teaches that even a very conservative substitution may abolish binding or may have very little effect on the binding affinity (see pg. 35, top of left column and pg. 33, right column). It is unlikely that a humanized immunoglobulin heavy chain or a humanized immunoglobulin light chain, which contain less than the full complement of CDRs from the heavy and light chain variable regions in their proper order and in the context of framework sequences

which maintain the correct spatial orientation for antigen recognition have the required CCR2 binding function. There is no guidance or direction provided in the specification to assist the skilled artisan in using humanized immunoglobulin heavy chains or humanized immunoglobulin light chains having specificity for CCR2. Further, a portion of the human IgG1 constant region (i.e., portion of SEQ ID NO:110) encompasses a myriad of fragments of the heavy chain constant region, which can be any one of the constant regions (CH1-3) and also may be the hinge region. However, the language also reads on small amino acid sequences, which are incomplete regions of the constant regions of the antibody. The specification does not provide sufficient guidance or direction as to the general tolerance to modification and extent of such tolerance; the specific portions of the constant regions which can be predictably modified and which portions are critical for maintaining antibody specificity for CCR2. One of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed.

In view of the lack of the predictability of the art to which the invention pertains as evidenced by Paul, Rudikoff et al and Coleman, the lack of guidance and direction provided by applicant, and the absence of working examples, undue experimentation would be required to practice the claimed veneered variable domains that bind antigen with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed veneered variable domains and absent working examples providing evidence which is reasonably

predictive that the claimed veneered variable domains bind antigen, commensurate in scope with the claimed invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaRosa et al [a] (US Patent 6,727,349 B1, priority to 2/3/2000) in view of Bonnefoy et al (WO 99/58679, 11/18/1999).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims are interpreted as being drawn to a humanized immunoglobulin having CCR2 specificity and comprising a heavy chain sequence comprising the variable heavy domain of SEQ ID NO:17 and the human IgG1 constant region of SEQ ID NO:110 and a light chain sequence comprising the variable light domain of SEQ ID NO:12 and the human kappa constant region (Ck) and the humanized immunglobulin

comprises two heavy chains and two light chains. Further, the claims are interpreted as being drawn to a humanized antigen-binding fragment comprising the F(ab')2 fragment (i.e., CH1 and hinge) of the human IgG1 constant region of SEQ ID NO:110 and the human kappa constant region (Ck) and comprising two heavy chains and two light chains.

LaRosa et al [a] teach a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising the heavy chain variable domain of SEQ ID NO:17 and a light chain variable domain of SEQ ID NO:12 (see entire document, particularly columns 18-19 and claim 29) and a human IgG1 heavy chain constant region and a human kappa constant region (see column 19, lines 24-38) for treating a variety of human disorders in which activation of CCR2 by binding of chemokines is implicated (see columns 43-46). As a property is inherent to a product, the light chain human kappa constant region of LaRosa [a] necessarily comprises the amino acid sequence of SEQ ID NO:112, i.e., the amino acid sequence of the human kappa constant region. LaRosa et al [a] does not specifically teach a humanized CCR2 specific antibody or antigen-binding fragment thereof comprising the modified human IgG1 heavy chain constant region of SEQ ID NO:110. This deficiency is made up for in the teachings of Bonnefoy et al.

Bonnefoy et al teach a humanized antibody comprising a mutated IgG1 constant region lacking cytotoxicity and comprising an amino acid sequence of SEQ ID NO:110 and wherein the humanized antibody comprises a human kappa constant region (see pages 7 and 33 and Fig. 4).

It would have been *prima facie* obvious at the time of the claimed invention was made to have produced a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of LaRosa et al [a] and Bonnefoy et al because LaRosa et al [a] teach a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising the heavy chain variable domain of SEQ ID NO:17 and a light chain variable domain of SEQ ID NO:12 for treating a variety of human disorders in which activation of CCR2 by binding of chemokines is implicated and suggests using a mutated constant region to minimize Fc receptor binding and/or ability to fix complement (i.e., reduced cytotoxicity) (see column 19, lines 31-38) and Bonnefoy et al teach a humanized antibody comprising a mutated human IgG1 constant

region lacking cytotoxicity (i.e., SEQ ID NO:110) and both LaRosa et al [a] and Bonnefoy et al teach humanized antibodies comprising the human kappa constant region. Therefore, one of ordinary skill in the art would have been motivated to use the modified human IgG1 constant region of Bonnefoy in the humanized CCR2 antibody of LaRosa [a], since it lacks cytotoxicity and hence, would be less immunogenic in human patients and LaRosa [a] explicitly suggests using a mutated constant region to minimize Fc receptor binding and/or ability to fix complement (i.e., reduced cytotoxicity). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of LaRosa et al [a] and Bonnefoy et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

9. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaRosa et al [b] (US Patent 6,696,550 B2, priority to 2/3/2000) in view of Bonnefoy et al (WO 99/58679, 11/18/1999).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims and their interpretation have been described supra.

LaRosa et al [b] teach a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising the heavy chain variable domain of SEQ ID NO:17 and a light chain variable domain of SEQ ID NO:12 (see entire document, particularly columns 19-20) and a human IgG1 heavy chain constant region and a human kappa constant region (see column 20, lines 17-31) for treating a variety of human disorders in which activation of CCR2 by binding of chemokines is implicated (see columns 44-48). As a property is inherent to a product, the light chain human kappa constant region of

LaRosa [b] necessarily comprises the amino acid sequence of SEQ ID NO:112, i.e., the amino acid sequence of the human kappa constant region. LaRosa et al [b] does not specifically teach a humanized CCR2 specific antibody or antigen-binding fragment thereof comprising the modified human IgG1 heavy chain constant region of SEQ ID NO:110. This deficiency is made up for in the teachings of Bonnefoy et al.

Bonnefoy et al teach a humanized antibody comprising a mutated IgG1 constant region lacking cytotoxicity and comprising an amino acid sequence of SEQ ID NO:110 and wherein the humanized antibody comprises a human kappa constant region (see pages 7 and 33 and Fig. 4).

It would have been *prima facie* obvious at the time of the claimed invention was made to have produced a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region

of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of LaRosa et al and Bonnefoy et al because LaRosa et al teach a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising the heavy chain variable domain of SEQ ID NO:17 and a light chain variable domain of SEQ ID NO:12 for treating a variety of human disorders in which activation of CCR2 by binding of chemokines is implicated and suggests using a mutated constant region to minimize Fc receptor binding and/or ability to fix complement (i.e., reduced cytotoxicity) (see column 19, lines 31-38) and Bonnefoy et al teach a humanized antibody comprising a mutated human IgG1 constant region lacking cytotoxicity (i.e., SEQ ID NO:110) and both LaRosa et al and Bonnefoy et al teach humanized antibodies comprising the human kappa constant region. Therefore, one of ordinary skill in the art would have been motivated to use the modified human IgG1 constant region of Bonnefoy in the humanized CCR2 antibody of LaRosa, since it lacks cytotoxicity and hence, would be less immunogenic in human patients and LaRosa explicitly suggests using a mutated constant region to minimize Fc receptor binding and/or ability to fix complement (i.e., reduced cytotoxicity). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of

CCR2 by binding of chemokines is implicated in view of LaRosa et al and Bonnefoy et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 9-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 10-16, 27-29, 36, 38-39, 42-43, 46-47, 50-52, 57 and 59-60 of U.S. Patent No. 6,727,349 B1 (LaRosa et al [a]) in view of Bonnefoy et al (WO 99/58679, 11/18/1999).

The instant claims and their interpretation have been described supra.

Claims 1-7, 10-16, 27-29, 36, 38-39, 42-43, 46-47, 50-52, 57 and 59-60 of U.S. Patent No. 6,727,349 B1 are drawn to humanized immunoglobulins and antigen-binding fragments thereof having binding specificity for CCR2 comprising the antigen binding region from monoclonal antibody 1D9 or comprising the CDRs of monoclonal antibody 1D9 and a light chain framework region derived from the light chain of the HF-21/28 antibody and a heavy chain framework region derived from the heavy chain of the human 4B4'CL antibody and wherein the humanized immunoglobulin comprises human constant region of the gamma type. Further, the humanized immunoglobulin or antigen-binding fragments thereof can compete with murine monoclonal antibody 1D9 for binding to CCR2. The claims are also drawn to humanized immunoglobulins or antigen-binding fragments thereof having binding specificity for CCR2 comprising the light chain variable region of SEQ ID NO:12 and/or the heavy chain variable region of SEQ ID NO:17. Claims 1-7, 10-16, 27-29, 36, 38-39, 42-43, 46-47, 50-52, 57 and 59-60 of U.S. Patent No. 6,727,349 B1 do not recite a humanized CCR2 specific antibody or antigen-binding fragment thereof comprising the modified human IgG1 heavy chain constant region of SEQ ID NO:110 and a human kappa constant region (SEQ ID NO:112). These deficiencies are made up for in the teachings of Bonnefoy et al.

Bonnefoy et al have been described supra.

The claims in the instant application are obvious variants of claims 1-7, 10-16, 27-29, 36, 38-39, 42-43, 46-47, 50-52, 57 and 59-60 of U.S. Patent No. 6,727,349 B1 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized CCR2 specific

antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of Bonnefoy et al because Bonnefoy et al teach a humanized antibody comprising a mutated human IgG1 constant region lacking cytotoxicity (i.e., SEQ ID NO:110) and the human kappa constant region. Therefore, one of ordinary skill in the art would have been motivated to use the mutated human IgG1 constant region and kappa constant region of Bonnefoy in the recited humanized CCR2 antibodies comprising the heavy and light chain variable domains of SEQ ID Nos:17 and 12, respectively, since it lacks cytotoxicity and hence, is less immunogenic in human patients. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a humanized

CCR2 specific antibody and antigen-binding fragments thereof comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated, which is a species that reads upon the genus claims in US Patent 6,727,349 B1.

Claims 9-11 are directed to an invention not patentably distinct from claims 1-7, 10-16, 27-29, 36, 38-39, 42-43, 46-47, 50-52, 57 and 59-60 of U.S. Patent No. 6,727,349 B1. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 6,727,349 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon

the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
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SUPERVISORY PATENT EXAMINER

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